

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:  
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## PCT

### WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference <b>61506-PCT</b>		Date of mailing (day/month/year) <b>15 JUL 2003</b>
		<b>FOR FURTHER ACTION</b> See paragraph 2 below
International application No. <b>PCT/US04/20535</b>	International filing date (day/month/year) <b>24 June 2004 (24.06.2004)</b>	Priority date (day/month/year) <b>24 June 2003 (24.06.2003)</b>
International Patent Classification (IPC) or both national classification and IPC <b>IPC(7): C12Q 1/68; C07H 21/02, 21/04 and US Cl.: 435/6; 536/ 23.1 and 24.3</b>		
Applicant <b>JOHNS HOPKINS UNIVERSITY</b>		

1. This opinion contains indications relating to the following items:

- ☒ Box No. I      Basis of the opinion
- ☐ Box No. II      Priority
- ☒ Box No. III      Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV      Lack of unity of invention
- ☒ Box No. V      Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement
- ☐ Box No. VI      Certain documents cited
- ☐ Box No. VII      Certain defects in the international application
- ☐ Box No. VIII      Certain observations on the international application

#### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer <i>Maria J. Watts</i> Ethan Whisenant, Ph.D. Telephone No. (703) 308-0196
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WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/20535

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☒ table(s) related to the sequence listing

b. format of material

☐ in written format

☒ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE  
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International application No.

PCT/US04/20535

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 9-14 and 17

because:

☐ the said international application, or the said claim Nos. \_\_\_\_\_ relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 9-14 and 17 are so unclear that no meaningful opinion could be formed (*specify*):

Claim(s) 9-14 and 17 is/are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because these claim are indefinite in that they are improper multiple dependent claims.

☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. \_\_\_\_\_

☒ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form



has not been furnished



does not comply with the standard

the computer readable form



has not been furnished



does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.  
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**Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims <u>15-16</u>	YES
	Claims <u>1-8 and 18-23</u>	NO
Inventive step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-8, 15-16, and 18-23</u>	NO
Industrial applicability (IA)	Claims <u>1-8, 15-16 and 18-23</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

1. **Claim(s) 1-3, 5-8** lack novelty under PCT Article 33(2) as being anticipated by Herman et al. [US 5,786,146 (1998)].

Herman et al. teach a method for diagnosing cancer which comprises the detection of a variant of a SPARC nucleic acid molecule in a sample from a subject. Please note that any nucleic acid molecule can be said to be a variant of another nucleic acid molecule without more definition as to the metes and bounds of this terminology. Also, as regards the phrasing in Claims 5-8 which reads "wherein a methylated SPARC nucleic acid molecule **comprises** a sequence corresponding to SEQ ID No. 1 or **comprises** a sequence having at least about X%", any nucleic acid molecule can be said to comprise a sequence which corresponds to another nucleic acid molecule without more definition as to the metes and bounds of this terminology. A "sequence" can be as small as two nucleotides in length.

2. **Claim(s) 1-8** lack novelty under PCT Article 33(2) as being anticipated by Goggins et al. [WO 02/068694(2002)].

Goggins et al. teach a method for diagnosing pancreatic cancer which comprises the detection of a variant of a SPARC nucleic acid molecule in a sample from a subject. Please note that any nucleic acid molecule can be said to be a variant of another nucleic acid molecule without more definition as to the metes and bounds of this terminology. Also, as regards the phrasing in Claims 5-8 which reads "wherein a methylated SPARC nucleic acid molecule **comprises** a sequence corresponding to SEQ ID No. 1 or **comprises** a sequence having at least about X%", any nucleic acid molecule can be said to comprise a sequence which corresponds to another nucleic acid molecule without a definition as to the metes and bounds of this terminology. Finally, note that a "sequence" can be as small as two nucleotides in length.

3. **Claim(s) 15-16** lack novelty under PCT Article 33(2) as being anticipated by Kimchi [US 6,255,293(2001)].

Kimchi teach treating a patient with cancer with a therapeutically effective amount of a demethylating agent. One of the possible demethylating agent, taught by Kimchi is 5-aza-cytidine. Please note that without more a phrase a methylated SPARC molecule reads on any other gene. While the claims are interpreted in light of the specification, limitations from the specification are not read into the claims.

4. **Claim(s) 1-8 and 15-16 and 18-23** meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

## NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### "Statement under Article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

**It must be in the language in which the international application is to be published.**

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments and any accompanying statement, under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the time of filing the amendments (and any statement) with the International Bureau, also file with the International Preliminary Examining Authority a copy of such amendments (and of any statement) and, where required, a translation of such amendments for the procedure before that Authority (see Rules 55.3(a) and 62.2, first sentence). For further information, see the Notes to the demand form (PCT/IPEA/401).

### Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see the *PCT Applicant's Guide*, Volume II.